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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,453	10/02/2001	Shulamit Eyal	20174C-002410US	9637
20350	7590	12/18/2008	EXAMINER	
TOWNSEND AND TOWNSEND AND CREW, LLP			COOK, LISA V	
TWO EMBARCADERO CENTER				
EIGHTH FLOOR			ART UNIT	PAPER NUMBER
SAN FRANCISCO, CA 94111-3834			1641	
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			12/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/970,453	EYAL ET AL.	
	Examiner	Art Unit	
	LISA V. COOK	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 05 December 2008.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1,3,4,7 and 10-13 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1, 3, 4, 7, and 10-13 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. _____.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.

5) Notice of Informal Patent Application

6) Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/5/08 has been entered.

2. Currently claims 1, 3-4, 7, and 10-13 are pending and under consideration. Claims 2, 5-6, 8-9 and 14-18 have been previously canceled at Applicants request.

3. Objections and/or rejections of record not reiterated below have been withdrawn.

NEW GROUNDS OF REJECTIONS NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 3, 4, 7, and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is vague and indefinite because it is not clear as to what is being measured. In step c, a velocity dependence measurement of the characteristic parameter is determined. However, it is not clear as to how this measurement relates to the measurement in steps b or d. If it is applicants intent to merely confirm that the measurement in step b is velocity dependent and therefore requires the normalization of step d, that should be clearly outlined in the instant claims in order to obviate this rejection. Appropriate correction is required.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 1, 3, and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kopf-Sill et al. (US Patent #6,613,512) or Kopf-Sill et al. (US Patent #6,524,790) in view of van der Moolen et al. (Journal of Chromatography A, Vol.744, 1996, pages 103-113) and further in view of Crabtree et al. (Analytical Chemistry, 1999, 71, 2130-2138).

Kopf-Sill et al. disclose methods and microfluidic devices to measure reactants and reaction products while considering velocity. See column 1 line 64 through column 2 line 23.

Reactants and products with different velocities (characteristics of an analyte) are measured in a microfluidic channel. See column 2 lines 36-37 and lines 57-58. In one embodiment the fluid samples are transported from a first position to a second position by electroosmotic flow (claim 4). See column 6 lines 15-18. The time dependent data generated is processed to include baseline subtraction and masking for accurate measurements of the analyte of interest (normalizing and considering velocity). See column 1 lines 64-67 and column 22 lines 18-42.

Multiple detection positions/zones are taught at two different time points in figure 1. See figure 1 - Time=t2 and Time=t4 (time difference measurement). The time difference and velocity are utilized in an equation to accurately measure the characteristic of interest in the analyte (claims 8 and 9). See column 5 line 11 through column 6 line 43.

The various reactants and products can be assessed serially (individually) or simultaneously in the methods (claim 5). See column 2 lines 34-35. Kopf-Sill et al. teach the step of normalizing or eliminating the velocity component in reaction measurements. See column 5 lines 55-62 and column 8 lines 10-22.

Kopf-Sill et al. and Kopf-Sill et al. differ from the instant invention in not teaching sample velocity normalization as exemplified in the disclosure on page 7 lines 25-29. In particular the normalization is calculated by peak area multiplied by velocity.

However, van der Moolen et al. disclose that electrokinetic samples introduce bias due to the electrophoretic mobility of the substances. Therefore a correction by multiplying the peak area with the migration time is often deemed necessary. See abstract. van der Moolen et al. teach the dependence of the peak area on the velocity of the component as well as peak correction by multiplying the peak with the velocity. In other words, the dependence of peak area on velocity is taught on page 106. The reference demonstrated that normalization procedures will not only correct for differences in velocity between the components or variations in migration times, but will also offer the possibility to compare the results of experiments, performed under different circumstances. See page 104, 2nd column 2nd paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use normalize velocity as taught by van der Moolen et al. in either method of Kopf-Sill et al. (6,613,512 or 6,524,790) because van der Moolen et al. taught that normalization procedures will not only correct for differences in velocity between the components or variations in migration times, but will also offer the possibility to compare the results of experiments, performed under different circumstances. See page 104, 2nd column 2nd paragraph.

Kopf-Sill et al. and Kopf-Sill et al. in view of van der Moolen et al. differ from the instant invention in not teaching sample detection at a plurality of detection zones between a first position (sample entry time) and a second position (sample end time).

However, Crabtree disclose a particle detection method, which converts multiple-point (Shah function) time dependent measurements into fluorescence frequencies allowing for the viewing of analyte speed (applicants velocity). See abstract.

The SCOFT (Shah convolution Fourier transform detection) principal is utilized in a system comprising multiple detection slits that detect the sample fluorescence at varied times ($t=0$ through $t=t_4$) during the flow of sample through a column or channel. For example, See figure 1 and page 2131. The particle is constantly interrogated (measured) at a number of evenly spaced points (slits or zones) along the column or channel simultaneously by a single detector and the signals measured from all of these points along the column are summed. See page 2131, 1st column, 3rd paragraph. This procedure advantageously isolated the analyte peak from interferences such as baseline drift and line noise. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use dual detection zones, slits, spaced zones (plurality of different detection zones) as taught by Crabtree et al. in either method of Kopf-Sill et al. (6,613,512 or 6,524,790) in view of van der Moolen et al. because Crabtree et al. taught that dual detection zones, slits, spaced zones advantageously isolated the analyte peak from interferences such as baseline drift and line noise. See abstract.

One of ordinary skill in the art would have been motivated to utilize dual detection zones (plurality of different detection zones) in order to more accurately detect the particles of interest.

II. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kopf-Sill et al. (US Patent #6,613,512) or Kopf-Sill et al. (US Patent #6,524,790) in view of van der Moolen et al. (Journal of Chromatography A, Vol.744, 1996, pages 103-113) and further in view of Crabtree et al. (Analytical Chemistry, 1999, 71, 2130-2138) as applied to claims 1, 3, and 4 above, and further in view of Squire et al. (Journal of Microscopy, 197(2) 2/2000, 136-149).

Please see Kopf-Sill et al. (US Patent #6,613,512) or Kopf-Sill et al. (US Patent #6,524,790) in view of van der Moolen et al. and further in view of Crabtree et al. as set forth above.

Kopf-Sill et al. (US Patent #6,613,512) or Kopf et al.-Sill (US Patent #6,524,790) in view of van der Moolen et al. and further in view of Crabtree et al. differ from the instant invention in failing to teach acousto-optic modulators.

However, Squire et al. teach methods for measuring fluorescence with wave acoustic-optic modulators placed in a series. This configuration analyzed multiple data sets simultaneously and distinctly. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use acoustic-optic modulators as taught by Squire et al. in either method of Kopf-Sill et al. (6,613,512 or 6,524,790) in view of van der Moolen et al. and further in view of Crabtree et al. because Squire et al. taught that “standing wave acoustic-optic modulators provide a means of modulating a continuous wave laser in a sinusoidal manner at high frequencies.

A number of these [lasers] can be employed in series to simultaneously modulate the excitation light of individual frequencies, their differences, and sums.” See page 139 figure 2 and 2nd column last paragraph.

One of ordinary skill in the art would have been motivated to utilize these lasers in order to detect multiple frequencies simultaneously. There in evaluating several analytes.

III. Claims 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kopf-Sill et al. (US Patent #6,613,512) or Kopf-Sill et al. (US Patent #6,524,790) in view of van der Moolen et al. (Journal of Chromatography A, Vol.744, 1996, pages 103-113) and further in view of Crabtree et al. (Analytical Chemistry, 1999, 71, 2130-2138) as applied to claims 1, 3, and 4 above, and further in view of Armstrong et al. (Cytometry, 40:102-108, 2/2000).

Please see Kopf-Sill et al. (US Patent #6,613,512) or Kopf-Sill et al. (US Patent #6,524,790) in view of van der Moolen et al. and further in view of Crabtree et al. as set forth above.

Kopf-Sill et al. (US Patent #6,613,512) or Kopf et al.-Sill (US Patent #6,524,790) in view of van der Moolen et al. and further in view of Crabtree et al. differ from the instant invention in failing to teach oligonucleotide detection including nucleotide measurements.

However, Armstrong et al. teach this limitation. Their methods evaluate PCR probes that are linked to fluorescent molecules and measured by flow cytometry. See abstract. The method detects individual nucleotides from individual nucleotide fluorescence peaks. See figures 2, 3, and 4.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use detect oligonucleotides and the nucleotides which make up the oligonucleotides as taught by Armstrong et al. in either method of Kopf-Sill et al. (6,613,512 or 6,524,790) in view of van der Moolen et al. and further in view of Crabtree et al. because Armstrong et al. taught that genetic diversity is exhibited in disease and drug response and they can be effected by a single nucleotide difference/change/variant. See abstract.

Response to Arguments

6. Applicant contends that the combination of Kopf-Sill (US Patent #6,613,512) or Kopf-Sill et al. (US Patent #6,524,790) in view of Crabtree et al. does not make the instant invention obvious. Specifically, Applicant argues that the patents to Kopf-Sill et al. do not teach characteristic parameters that are independent of velocity flow. However, van der Moolen et al. have been added to demonstrate that velocity measurements may be normalized to provide results which are independent of the flow velocity.

With respect to the rejections under 35 USC 103(a), including Squire et al. (Journal of Microscopy, 197(2) 2/2000, 136-149) and Armstrong et al. (Cytometry, 40:102-108, 2/2000), applicant contends that the additional references do not cure the deficiencies of Kopf-Sill or Kopf-Sill et al. in view of Crabtree et al. The rejection over Kopf-Sill or Kopf-Sill et al. in view of Crabtree et al. has been addressed above. Therefore the rejections are maintained.

6. For reasons aforementioned, no claims are allowed.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, can be reached on (571) 272-0806.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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